

FIG. I A-1

Signal peptide →

Pro-peptide →

→ MMP-1 MMP-2 MMP-3 MMP-7 MMP-8 MMP-9 MMP-10 MMP-11 MMP-12 MT-MMP-1 MT-MMP-3 Consensus

DAETLKVMKQPRCGVPDVVAQ---
DQNTIETMRKPRCGNPDVAN---
DSDTLEVMRKPRCGVPDVGH---
NSRVIEIMQKPRCGVPDVAE---
NEETLDMMKPRCGVPDSGG---
DSATLKMAMRTPRCGVPDILGR---
DTDTLEVMRKPRCGVPDVGH---
APRPASSLRRPPRCGVPDPSD---
DTSTLEMMMAHAPRCGVPDILHH---
DADTMKAMRRPRRCGVPDKFGAEIKANVRKRYAIQ-G-LKWHQHNEIT
DRNTIDWMKKPRCGVPDQTRGSSKFHIRRKRYALTGQ--KWHQHKHIT
D...TL..MRKPRCGVPD...F...PG.PKH...T

→ IS-1

FIG. 1A-2 Pro-peptide

EQDV/DLVQKYLEKYYNLKNDGROVEKRRNSGPVV-EKLKQMQUEFFGLKVTGKP 79
 DVAPK-TDKEELAVQYLNTF-YGCCPKE-SCNLFVILKDTLKKMQKFGLPQTGDL 89
 DTSMLNLYQKYLENYDLKKDVKQFVRRKDSCGPVV-KKIREMQKFGLGLEYTGKL 79
 AGHMSSELQWEEQAQDY-LKRFYLYDSETKNANSLE-AKLKEMQKFGLPITGML 74
 EKNTKTVQDYLEKFYQLPNSNQYQSTR-KNGTNVIVEKLKEMQRFEGLNVTGKP 78
 DLRTNLTDRLAEEYLYRYGYTRVAEMRGESKSISGPALLLQKQQLSLPETGEL 86
 DSNKDLAQQYLEKYYNLKDVQFRRK-DSNLIV-KKIQGMQKFGLGLEYTGKL 78
 PDVHHLHAERRGPQ-----PWHAALPSSPAPAPATQE 67
 KNNVLFGERYLEKFYGLEINKLPVTKMKYSGNIMKEKIQEMQHFLGLKVTGQL 79
 -----EAWLQQYGYLPPGDLRTHTQRSQSLS-AAIAAMQKFYGLQVTGKA 80
 TEQYFNVEWNLQKYGYLPPTSRMSVVRSAETMQ-SALAAMQQFYGINMTCKV 88
 -----KL-----KL-----KL-----KL-----KL-----KL-----KL 100

Catalytic 160 YRIENYTPDLPRADVVDHAIKEKAFOQLWSNVTPLTFTKV-----SEGQADIM
YRIIGYTPDLDPETVDDAFARAFQVWSDVTPLRFsRI-----HDGEADIM 170
YRIVNYTPDLPKDAVDSAVEKALKVWEEVTPLTFSRL-----YEGEADIM 160
YRIVSYTRDLPHITVDRLLWSKALNMWGKEIPLHFRKV-----VWGTADIM 155
YRIRNYTPQLSAEVERAIKDAFELWSVASPLIFTRI-----SQGEADIN 159
YWIQNYSEDLPRAVDDAFARAFALWSAVTPLTFTRV-----YSRDA DIV 167
YRIVNYTPDLPRDAVDSALEKALKVWEEVTPLTFSRL-----YEGEADIM 159
YRILRFPWQOLVQEQRQTMAEAALKVWSDVTPLTFTEV-----HEGRADIM 156
YRINNYTPDMNREDVDYAIRKAFOQVWSNVTPLKFSKI-----NTGMADIL 160
FCIONYTPKVGEYATYEAIRKAFRVWEATPLRFREVPYAYIREGHEKQADIM 178
YSIKNVTPKVGDPETRKAIRRAFDVWQNTVPLTFFEVPSLENGK-RDVDIP 185
YDIINYTPDRI VD AI KAE VWS VTPLTFSRL-----G.ADIM 200

FIG. 1B-1

Catalytic

MMP-1
MMP-2
MMP-3
MMP-7
MMP-8
MMP-9
MMP-10
MMP-11
MMP-12
MT-MMP-1
MT-MMP-3
Consensus

ISFVRGDDHRDMSPFDCPGGNILAHAFQPGPGIGGDAHFDEHERWTN-NFTEYN
INFGRWEHGDGYPFDCGKDGGLILAHAFAPGTVGGDSHFDDDELWTLGEQVVR
ISFAVREHGDFYPFDCPGNVILAHAFAPGPGINGDAHFDDDEQWTK-DTTGTN
IGFARGAHGDSYPFDCPGNTILAHAFAPGTGLGGDAHFDEDERWTDGSSLGIN
IAFYQRDHGDNNSPFDCPGNGILAHAFQPGQGIGGDAHFDAEETWTN-TSANYN
IQFGVAEHGDGYPFDCGKDGGLILAHAFPPGPGLQGDAHFDDDEKWT-EASGTN
ISFAVKEHGDFYSFDCPGCHSILAHAYPPGPGLYCDIHFDDEKWT-EASGTN
IDFARYWDGDDLPFDCPGGILAHAFFPKTHREGDVHFDYDETWТИGDDQGTD
VVFARGAHGDFHAFDGKGGILAHAFPGSGSIGGDAHFDEDEFWTT-HSGGTN
IFFAEGFHGDSTPFDCEGGFILAHAYPEPGPNIGGDTHFDSAEPWTV-RNEDLN
IIIFASGFHGDSSPFDCEGGFILAHAYPEPGPNIGGDTHFDSDEPWTLGNPNHDG
I.FA...HGD..PFDGPGG.LAHAF.PGPGIGGDAHF.DE.WT.-...N

Catalytic

MMP-1
MMP-2
MMP-3
MMP-7
MMP-8
MMP-9
MMP-10
MMP-11
MMP-12
MT-MMP-1
MT-MMP-3
Consensus

YGFCPHEALFTMGGNAEGQPKFPRFQGTSYDSCTTEGRTDGYRWCGTTED

FGFCPSERLYTRDGNADGXPCQFPFIQGQSYSACTTDGRSDGYRWCGATTAN

FIG. 1B-2

211
V KYGNADGEYCKFPFLNGKEYNSCTDTGRSDGFLWCSTTYNFEKDGK
270
211
207
210
TRFGNADGAACHFPFIFEGRSYSACTTDGRSDGLPWCSTTANYDTDDDR
267
210
208
211
229
237
300

211
YDRDKKYGFCPETAMSTV-GGNSEGAPCVFPFTFLGNKYESCTSAGRS
369
211
207
210
YDRDKLFGFCPTRADSTVMGGNSAGELCVFPFTFLGKEYSTCTSEGRG
367
210
208
211
229
237
400

FIG. IC-1

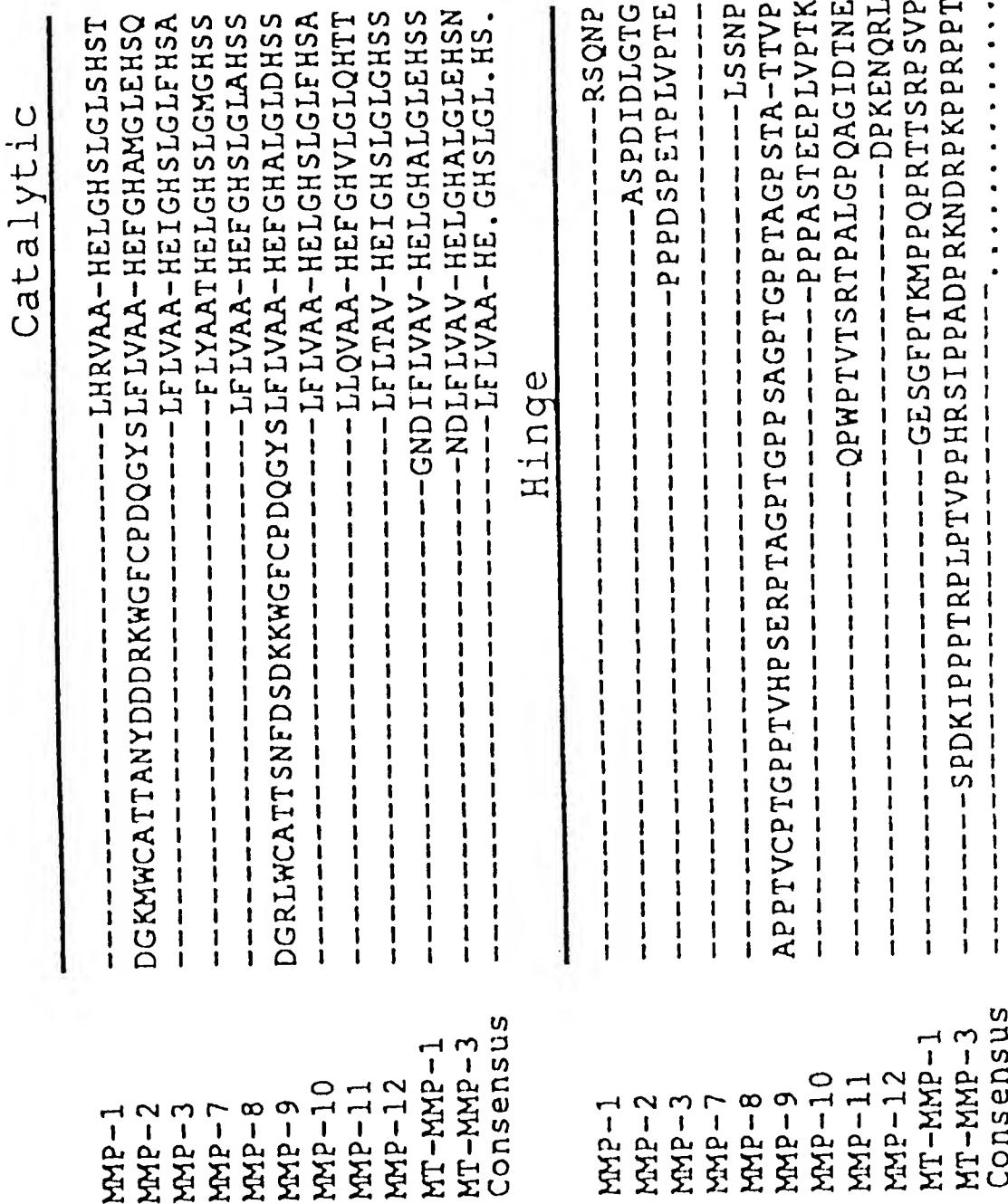


FIG. IC-2

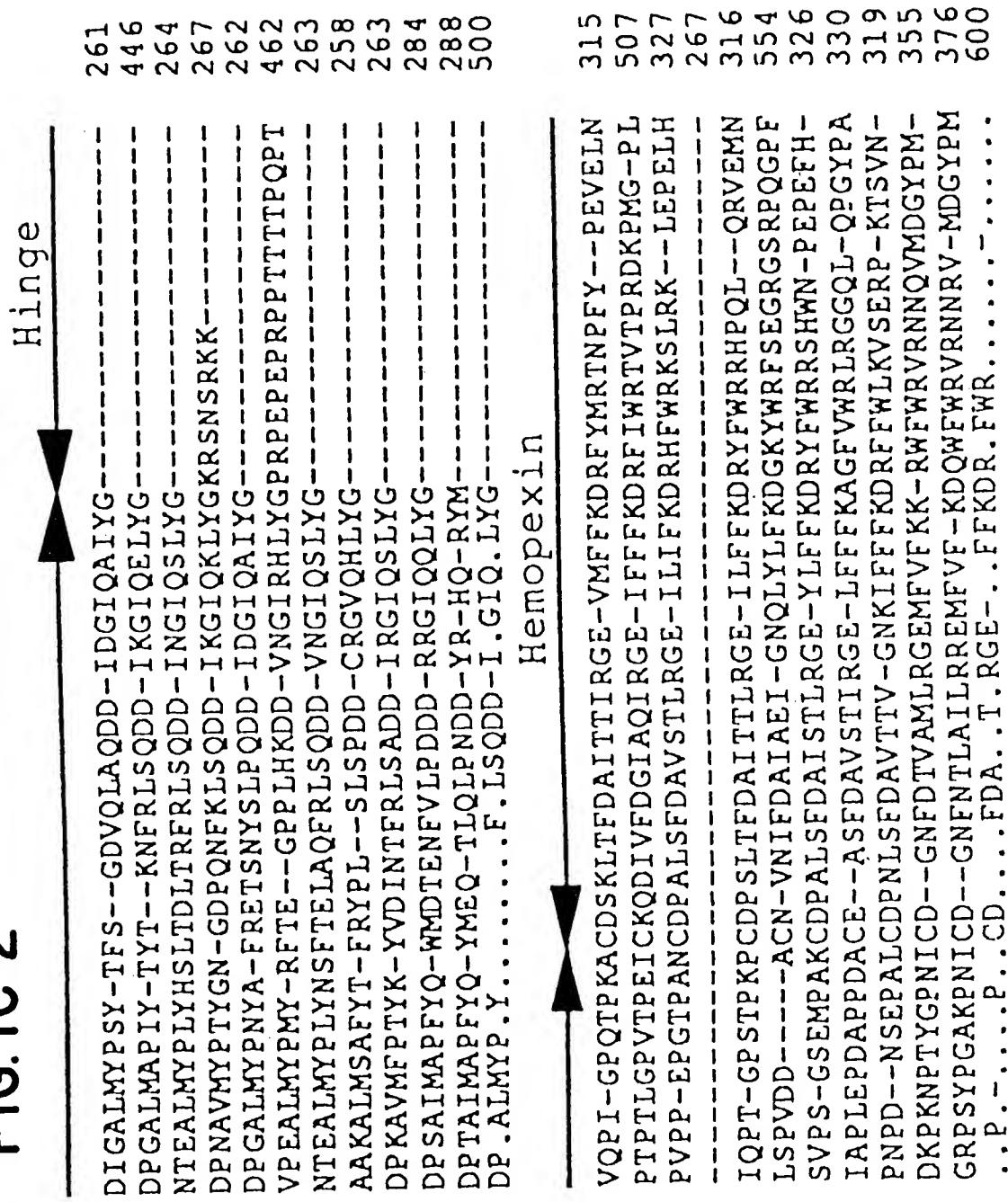


FIG. 1D-1

Hemopexin

MMP-1	FTSVFWPQLPNGLEAAAYEADRDEVRF	F	KGNKYKAV	-QGQNVLHGY	P	KDIYSSFGFPR	
MMP-2	LVATEFWPELPEKIDAVYEAPQEEKAVF	E	AGNEYWIY	-SASTLERGY	P	KPLTS-LGLPP	
MMP-3	LISSFWPSLPSGVDAAYEVTSKDLVF	I	F	KGNQFWAI	-RGNEVRAGY	P	RGIHT-LGFPP
MMP-7	-----	-----	-----	-----	-----	-----	-----
MMP-8	FISLFWPSLPTGIQAAAYEDFDRLLIF	K	FGNQYWL	-SGYDILQGY	P	KDISN-YGFPS	
MMP-9	LIADDKWPALPRKLDVSFEEPLSKLFFF	S	GRQVWVYT	GASVL-G	P	RRLDK-LGLGA	
MMP-10	LISAFWP SLPSYLDAAYEVNSRDTVF	I	F	KGNEFWAI	-RGNEVQAGY	P	RGIGHT-LGFPP
MMP-11	LA SRH WQGLPSPVDAAFE-DAQGH	I	WFF	FQGAQY	WVY	DGEKPVLG-P	APLIE-LGLVR
MMP-12	LISSLWPTLPSGIEAAYEIEARNQV	F	FLFKDDK	YWL	I-SNLR	PEPNYPSKSIHS-F	GFPPN
MT-MMP-1	PIQQFWRGLPASINTAYERKDGF	K	FVF-F	KGDKH	WVF	DEASLEPGYP	KHIKE-LGRGL
MT-MMP-3	QITYFWRGLPPSIDAVYENSDGN	E	VVF-F	KGNKY	WVF	KDTTLQPGYP	HDLIT-LGSGI
Consensus	LIS.FWP.LP...	DAAYE...	VF.FKGN.YW...	GYP.I...	-LG.P.

Hemopexin

MMP-1	MIAHDFPGIGHKVDAVFMKDGF	F	YFFHGTRQYKFD	PKT-KRIL	TL-QKAN	S-WFNC
MMP-2	LIADAWNAPIPDNLDAVVLQGGH	SYFF	KGAYYLKLEN	Q	SSELNQVDQV	YVTDILQC
MMP-3	QIAEDFPGIDSKIDAVFEEFGF	--YFF	TGSSQLEFD	PKNA-KKV	THT-LKSNS-WLNC	-WLNC
MMP-7	-----	-----	-----	-----	-----	-----
MMP-8	SISGAFPGIESKVD	Q	QEHF	F-HVFSGPRYYAF	DLIA-QRV	TRY-ARGNK-WLNC
MMP-9	EVDRMFPGVPLDTHDVFQYREKA	--YFCQDRF	Y	YWRVSSRSELNQVDQV	GYV	YDILQC
MMP-10	LIADDDFPGVEPKVDAVLQAF	GFF--YFF	SGSSQ	FEEDPNA-RMV	THI-LKSNS-WLHC	-WLHC
MMP-11	R-ATDWRGVPSEIDAAFQDAD	GYA-YFLRGR	LYWKF	DPK-VKALEG	FPRLVGP	DFFG
MMP-12	LITKNFQGIGPKIDAVFYSK	NQFEY	YD	YD	YD	YD
MT-MMP-1	NIKVWE-GIPESPRGSEMG	SDEVFTY	YKGNKY	WKFNNQKLKV	E PGYPKS	ALRDWMGC
MT-MMP-3	PITWTK-GIPESPQGAFVH	KENGFTY	YKEGVILE	IQTTRYSR	LEPGHPR	SILKDLSSGC
Consensus	I...F.GI....DAVF-YFF.G-FD-W..C

FIG. ID-2

TVKHIDAA-LSEENTGKTYFFVANKYWRYDEYKRSMDPGYPK	413
DVQRVDAA-FNWSKNNKTYIFAGDKFWRYNEVKKKMDPGFPK	604
TVRKIDAA-ISDKEKNKTYFFVEDKYWRFDEKRN SMEPGFPK	424
	267
SVQAIIDAA-VFYRS--KTYFFVNDQFWRYDNQRQFMEPGYPK	411
DVAQVTGA-LRSGR-GKMLLFSGRRILWRFDVKAQMVDPRSAS	648
TIRKIDAA-VSDKEKKKTYFFAADKYWRFDENQSMEQGFPR	423
FP--VHAALLVWGP EKNNKTYFFRGRDYWRFHPSSTRRVDSVPR	424
FVKIDAA-VENPREFYRTYEFFVDNQYKRYDERRQMMDPGYPK	416
PTDKIDAA-LFWMMPNGKTYFFRGNKYYRFNEELRAVDSEYPK	451
PPHGIDSA-IWWEDVUGKTYFFKGDRYWRYSEEMKTMMDPGYPK	472
.V..IDAA-.....KTYFF.....YWR.DE....MDPG.PK	700
RKN-----	469
	660
	477
	267
RYG-----	467
PED-----	707
	476
CAEPANTFL-----	488
	470
PSGGRPDEGTEEEETE-VIIIEEGGGAVSAAVVLPVLLL	549
DGPTDRVKEGHSPDDVDIVKLDNTASTVKAIAVIPCILA	571
	800

FIG. 1E

MMP-1 469
MMP-2 660
MMP-3 477
MMP-7 267
MMP-8 468
MMP-9 708
MMP-10 476
MMP-11 489
MMP-12 470
MT-MMP-1 582
MT-MMP-3 604
Consensus 833

LLVIAVGLAVFFRRHGTPRRLIYCQRSLLDKV
LCLLVLVYTVFQFKRKGTPRHILYCKRSMQEWV

FIG. 2

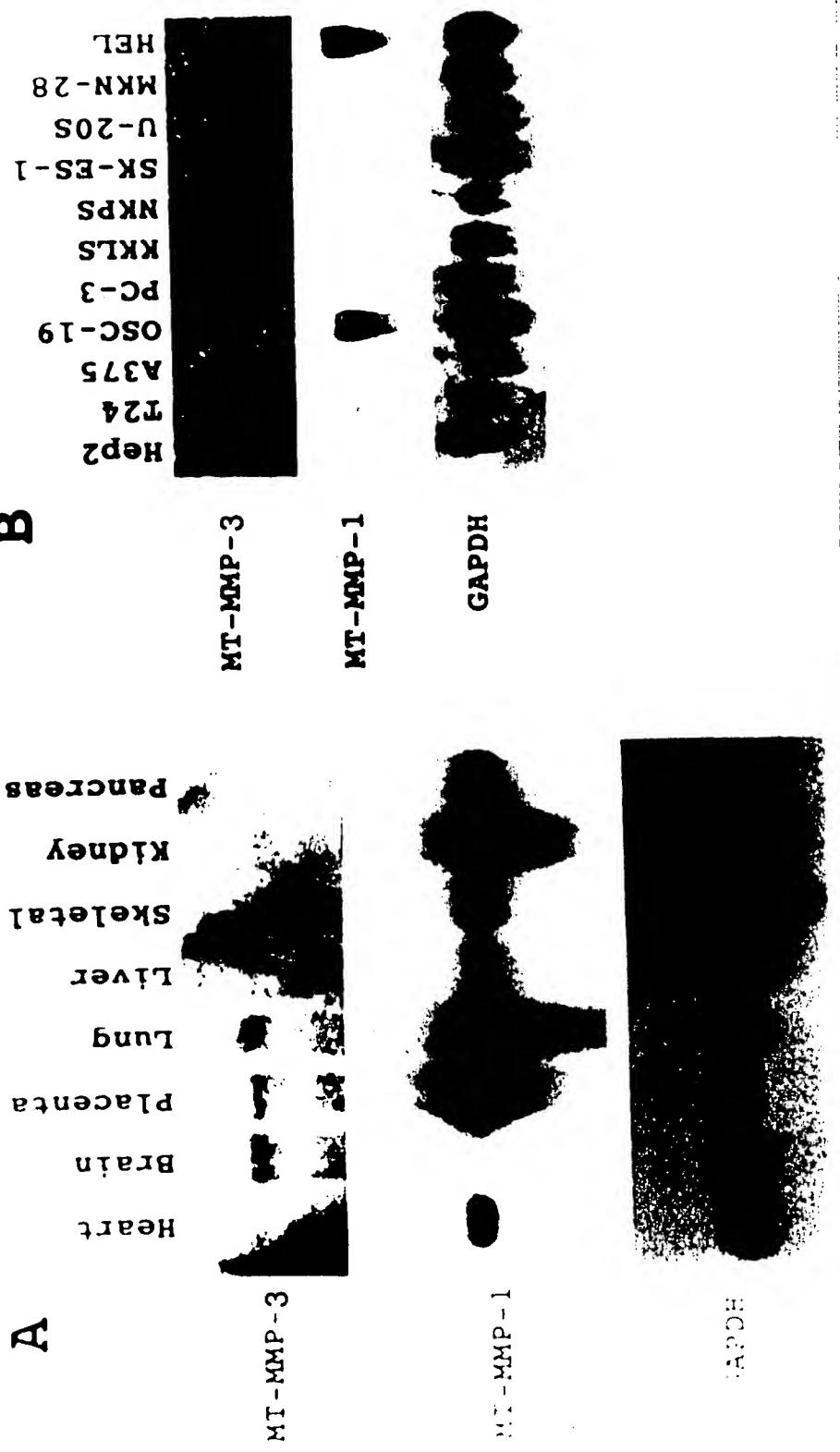


FIG. 3

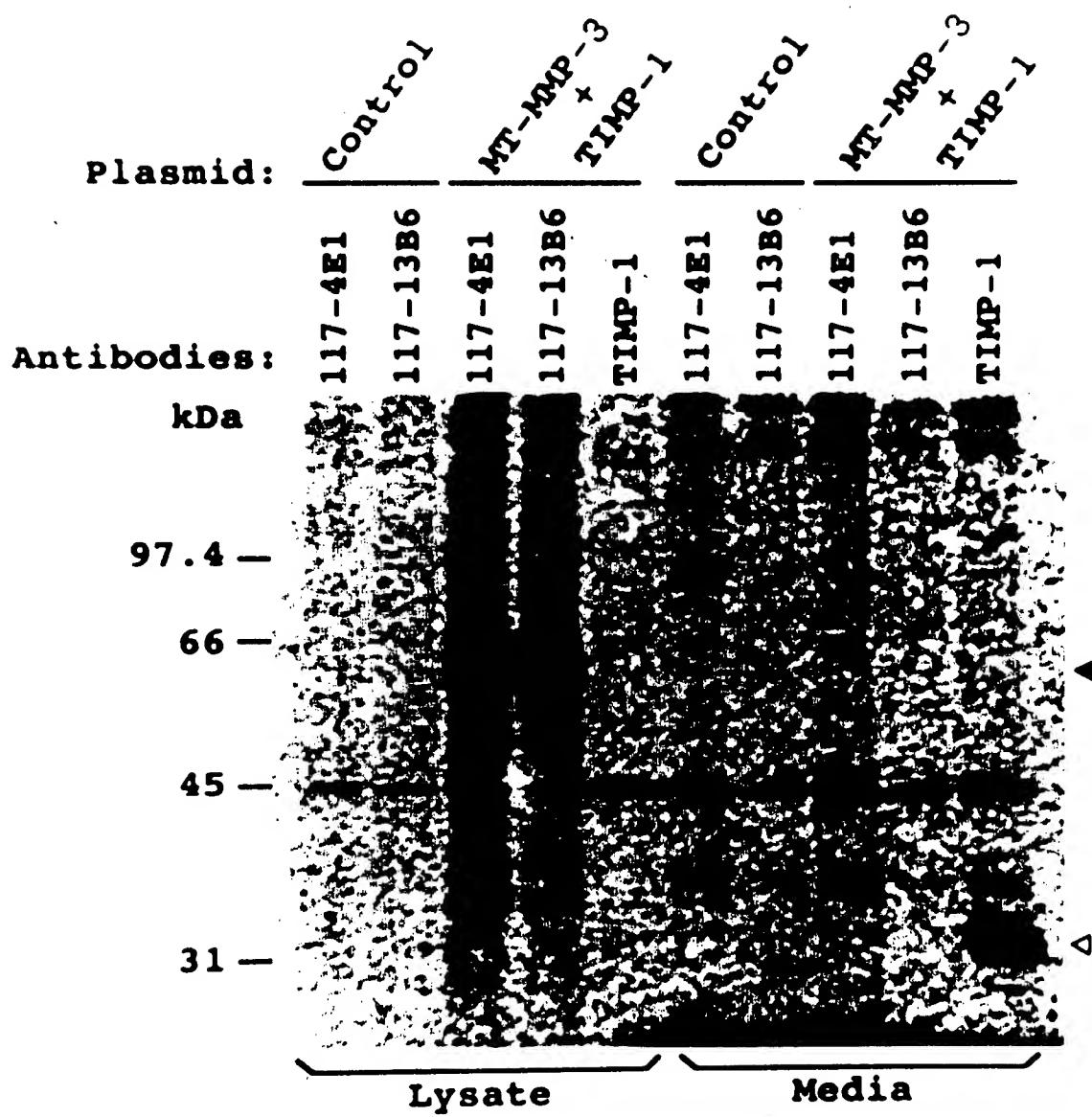
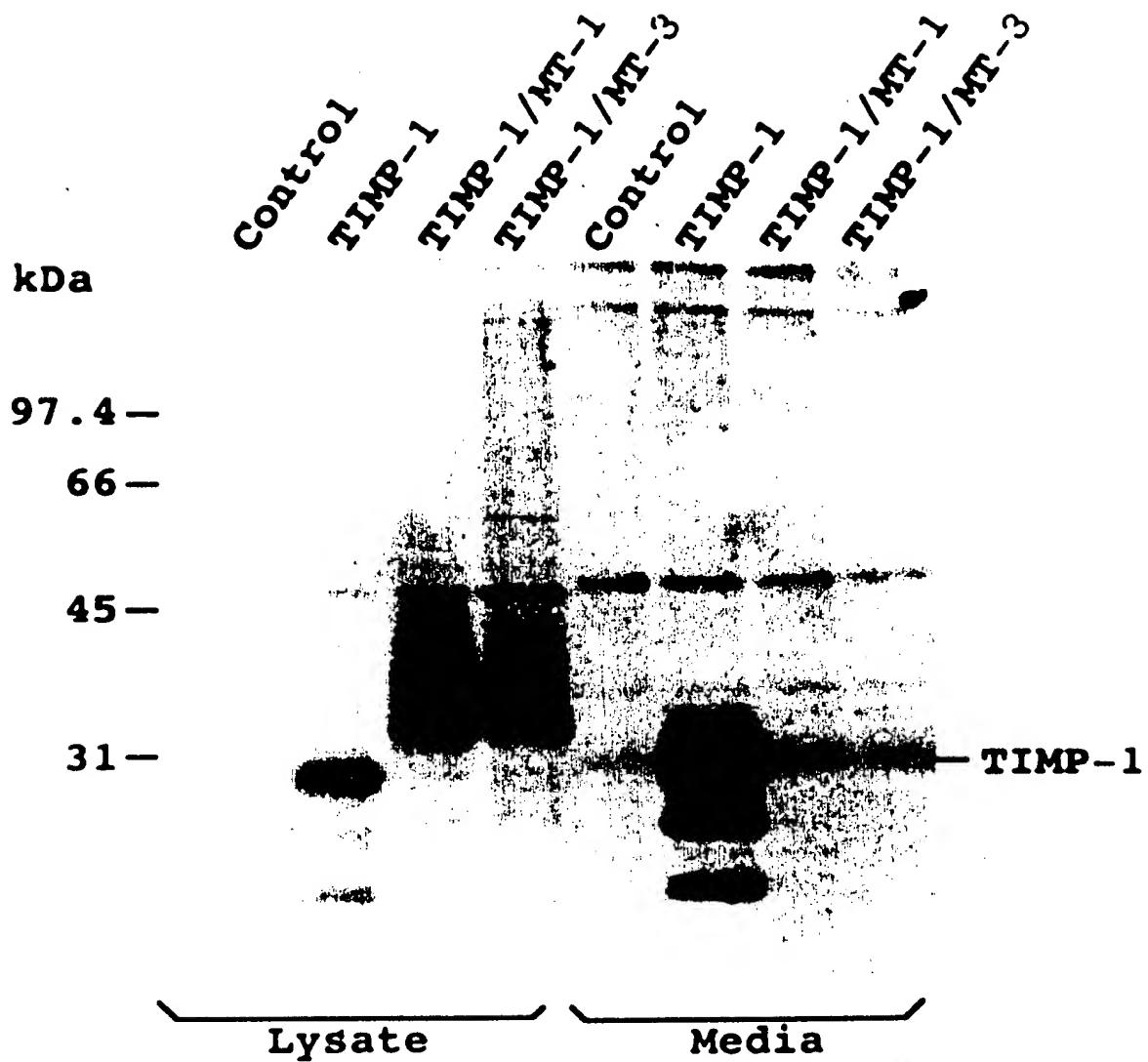


FIG. 4



5
FIG.

Control

TEMP-1/MT-3

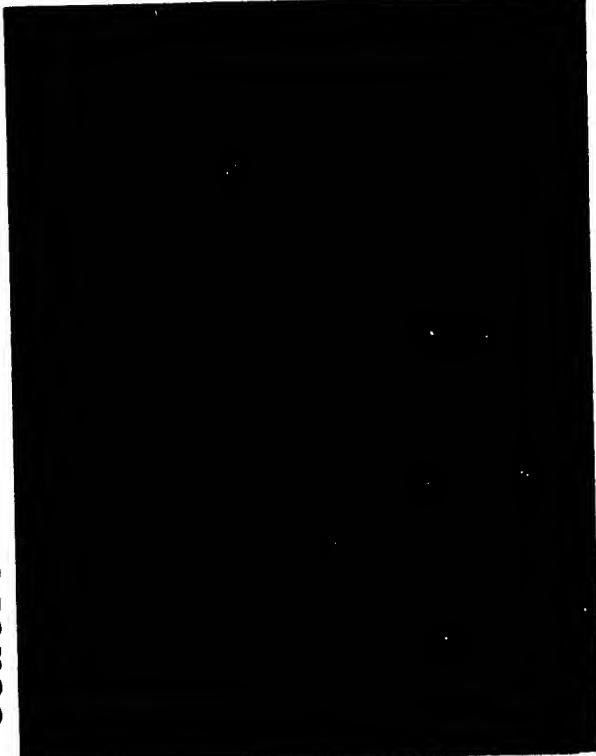


FIG. 6

